Is there an association between pain and magnetic resonance imaging parameters in patients with lumbar spinal stenosis?

Burgstaller, Jakob M ; Schüffler, Peter J ; Buhmann, Joachim M ; Andreisek, Gustav ; Winklhofer, Sebastian ; Del Grande, Filippo ; Mattle, Michèle ; Brunner, Florian ; Karakoumis, Georgios ; Steurer, Johann ; Held, Ulrike

DOI: https://doi.org/10.1097/BRS.0000000000001544

SPINE An International Journal for the study of the spine Publish Ahead of Print

DOI : 10.1097/BRS.0000000000001544

Is there an association between pain and magnetic resonance imaging parameters in patients with lumbar spinal stenosis?

Jakob M. Burgstaller M.D., D.M.D.[1], Peter J. Schüffler Ph.D.[2], Joachim M. Buhmann Ph.D.[2], Gustav Andreisek M.D., M.B.A.[3], Sebastian Winklhofer M.D.[3], Filippo Del Grande M.D.[3,4], Michèle Mattle MSc.[1], Florian Brunner M.D., Ph.D.[5], Georgios Karakoumis M.D.[6], Johann Steurer M.D.[1], Ulrike Held Ph.D.[1] on behalf of the LSOS Study Group

[1] Horten Centre for Patient Oriented Research and Knowledge Transfer, Department of Internal Medicine, University of Zurich, Pestalozzistrasse 24, 8032 Zurich, Switzerland
[2] Department of Computer Science, ETH Zurich, Universitätstrasse 6, 8006 Zurich, Switzerland
[3] Institute of Diagnostic and Interventional Radiology, University Hospital Zurich, University of Zurich, Ramistrasse 100, 8091 Zurich, Switzerland
[4] Department of Radiology, Regional Hospital, Via Tesserete 46, 6900 Lugano, Switzerland
[5] Department of Physical Medicine and Rheumatology, Balgrist University Hospital, Forchstrasse 340, 8008 Zürich, Switzerland
[6] Institute of Neurosurgery, Kantonsspital Winterthur, Brauerstrasse 15, 8401 Winterthur, Switzerland

Corresponding author:
Jakob M. Burgstaller, M.D., D.M.D.
Horten Centre for Patient Oriented Research and Knowledge Transfer, Department of Internal Medicine, University of Zurich, Pestalozzistrasse 24, 8091 Zurich, Switzerland
Phone: +41 44 255 87 09
Facsimile: +41 44 255 97 20
E-mail:jakob.burgstaller@usz.ch

Acknowledgement: September 10, 2015
1st Revise: November 17, 2015
2nd Revise: December 10, 2015
3rd Revise: February 1, 2016
Accept: February 2, 2016

The manuscript submitted does not contain information about medical device(s)/drug(s).
The Baugarten Foundation, the Helmut Horten Foundation, the Pfizer-Foundation for geriatrics & research in geriatrics, the Symphasis Charitable Foundation, and the OPO Foundation funds were received in support of this work.
No relevant financial activities outside the submitted work.

Abstract

Study design: Prospective multi-center cohort study.

Objective: To identify an association between pain and magnetic resonance imaging (MRI) parameters in patients with lumbar spinal stenosis (LSS).

Summary of Background Data: To the present, the relationship between abnormal MRI findings and pain in patients with LSS is still unclear.

Methods: First we conducted a systematic literature search. We identified relationships of relevant MRI parameters and pain in patients with LSS. Second, we addressed the study question with a thorough descriptive and graphical analysis to establish a relationship between MRI parameters and pain using data of the lumbar spinal stenosis outcome study (LSOS).

Results: In the systematic review including four papers about the associations between radiological findings in the MRI and pain, the authors of two articles reported no association and two of them did. Of the latters, only one study found a moderate correlation between leg pain measured by Visual Analogue Scale (VAS) and the degree of stenosis assessed by spine surgeons. In the data of the LSOS study we could not identify a relevant association between any of the MRI parameters and buttock, leg and back pain, quantified by the Spinal Stenosis Measure (SSM) and the Numeric Rating Scale (NRS). Even by restricting the analysis to the level of the lumbar spine with the most prominent radiological 'stenosis' no relevant association could be shown.

Conclusion: Despite a thorough analysis of the data we were not able to prove any correlation between radiological findings (MRI) and the severity of pain. There is a need for innovative 'methods/techniques' to learn more about the causal relationship between radiological findings and the patients' pain related complaints.

Key Words: magnetic resonance imaging; MRI; lumbar spinal stenosis; pain; low back pain; Spinal Stenosis Measure; VAS; NRS; association; relationship; SSM

Level of Evidence: 2

Introduction

Lumbar spinal stenosis (LSS) is the most frequent indication for spine surgery in patients older than 65 years.[1] The definition of LSS by the North American Spine Society − "[…] diminished space available for the neural and vascular elements in the lumbar spine secondary to degenerative changes in the spinal canal. When symptomatic, this causes a variable clinical syndrome of gluteal and/or lower extremity pain and/or fatigue which may occur with or without back pain. […]" − includes both clinical (neurogenic claudication) and radiological (morphological abnormalities) criteria.[2] To the present, the relationship between abnormal magnetic resonance imaging (MRI) findings and pain is still debated.[3-7] It has been shown that symptoms often poorly correlate with radiologic findings.[4] Ishimoto et al.[8] reported that a substantial number of asymptomatic persons showed a moderate or even severe narrowing of the spinal canal (defined as more than ⅓ or ⅔ area loss respectively) in the MRI. Two other studies also found asymptomatic patients, however, their patient samples were much smaller.[4,9] Nevertheless, MRI is broadly used in establishing the diagnosis of LSS. Furthermore, MRI is used for recommending treatment to patients with LSS, in particular, radiological findings are used for preoperative planning.

The aims of this article are 1) to systematically identify and analyze published articles on the relationship between MRI findings and pain in patients with lumbar spinal stenosis, and 2) to search for MRI parameters that are associated with pain using data of the LSOS (lumbar spinal stenosis outcome study).

Methods

The approach to answer the study questions uses a two-step approach. First, we conducted a systematic literature search to identify clinically relevant MRI parameters in patients with lumbar spinal stenosis. Second, we addressed the study question with a thorough descriptive and graphical analysis to establish a relationship between MRI parameters and pain using data of the first 150 patients of the lumbar spinal stenosis outcome study (LSOS) who had an MR image. The LSOS is a multi-centre prospective cohort study that includes patients with neurogenic claudication and

findings of lumbar spinal stenosis in MRI.[10] The LSOS was conducted in compliance with all international laws and regulations as well as any applicable guidelines. The study was approved by the independent Ethics Committee of the Canton Zurich (KEK-ZH-NR: 2010-0395/0).

Step 1 - Systematic literature review

Literature Search

We identified all studies meeting our eligibility criteria (defined in detail below) published in the last 15 years. The following databases were searched in May 2014: Cochrane Library, Embase, and Medline. The search was conducted by an experienced librarian. Search terms included various terms for MRI (e.g., magnetic resonance imaging, MR imaging, MRI) and questionnaires to assess pain (e.g. Spinal Stenosis Measure). The detailed search strategy in Embase is shown in **Appendix 1**. In addition, bibliographies of included studies relevant to the research question were searched and potential eligible references included in the full text review.

Eligibility Criteria

All studies were considered eligible for inclusion in further analyses that met the following criteria: the term "stenosis" must be mentioned in title or abstract, assessed the relationship between MRI parameters and validated questionnaires on pain in patients with symptomatic lumbar spinal stenosis. Studies were included if they were published within the last 15 years. No limits for the study setting or language of the publication were applied. Excluded were studies with patients of an age younger than 50 years, receiving or received any treatment, with neoplasia/cancer, fractures, injuries, infectious spine diseases, fibromyalgia, syndromes (e.g. Marfan syndrome), tuberculosis, cervical and thoracic spinal disorders, and examined/investigated by SPECT (single-photon emission computed tomography).

Study selection, data extraction and synthesis

The bibliographic details of all retrieved articles were stored in an EndNote file.[11] Two reviewers (xx and xx) independently screened all references by title and abstract. The full text of included studies was reviewed by both reviewers independently (xx and xx). Disagreements were discussed and resolved by consensus or by third party arbitration (xx). Alternative researchers with specific language proficiencies were used for non-English language references. In case of several publications for the same cohort without change in outcome or follow-up duration the most recent publication was chosen and missing information from the previous publication was added.

The search and inclusion/exclusion process is summarized in **Figure 1**. Out of 2030 records, 73 were reviewed in full text. For the final analysis we could include four publications. Reasons for the exclusion of 69 studies are provided in **Figure 1**.

Step 2 - Evaluation of association between pain and MRI parameters in patients of the LSOS study

Patient selection

The Lumbar Stenosis Outcome Study (LSOS) was conducted at eight medical centers (with approximately two million inhabitants in the catchment area) with Rheumatology and Spine Surgery Units in Switzerland. Patients with a history of neurogenic claudication and lumbar spinal stenosis verified by Magnetic Resonance Imaging (MRI) or Computer Tomography (CT) were eligible. Patients had no evidence of stenosis caused by tumor, fracture, infection, or significant deformity (>15° lumbar scoliosis), and were aged 50 years or more. None of the patients had prior lumbar spine surgery. Furthermore, patients had no clinical peripheral artery occlusive disease (confirmed by a vascular specialist in patients without palpable pulses in the lower limb).

MRI parameters

Data on 23 different MRI parameters, prospectively measured in each of the five lumbar spine levels, were available for each patient. The image analysis started at the superior endplate of the L1

and ended at the level of the vertebral disc L5/S1. Parameters, such as the compromise of the central zone, were assessed for each level at the height of the most severe stenosis, typically at the intervertebral disc level (e.g. L3/L4). Other parameters, such as vertebral body fracture, were evaluated at the corresponding vertebral body level (e.g. L3). The 23 parameters were measured in the context of the LSOS study because they were identified as important paramenters prior to the start of LSOS in a consensus meeting among experts in the field.[12] The list of parameters is shown in **Appendix 2**. Among those 23 parameters, Andreisek et al.[12] identified five core parameters which were: "compromise of central zone", "relation of fluid to nerve roots in the central canal", "nerve root compression in the lateral recess (right/left)", "compromise of the foraminal zone (right/left)", and "foraminal nerve root impingement (right/left)".

Definition of outcome measures (pain)

The instrument to quantify the outcome in the LSOS study is the pain domain of the Spinal Stenosis Measure (SSM) (also known as Swiss Spinal Stenosis Questionnaire, Zurich Claudication Questionnaire, or Brigham Spinal Stenosis Questionnaire)[13], a validated self-administered questionnaire for patients with lumbar spinal stenosis. We did not restrict our pain outcomes to the SSM, but included all relevant and validated questionnaires in the literature review. Among others, these included the Numeric Rating Scale (NRS), the visual analogue scale (VAS), and the McGill Pain Questionnaire (MPQ).

Subscales of the Spinal Stenosis Measure (SSM)

There are three subscales of the SSM: the symptom severity scale (seven items), the physical function scale (five items), and the satisfaction scale (six items). The symptom severity scale consists of two subdomains: pain domain (3 items) and neuroischemic (4 items). The SSM has been shown to be reproducible, internally consistent, valid, and reliable. The internal consistency ranged

from 0.64 to 0.92, the test-retest reliability from 0.82 – 0.96.[13,14] For the evaluation in this paper, we focused on pain subdomain of the SSM (SSM pain), ranging from 1-5 (best-worst).

Numeric Rating Scale (NRS)

The NRS is used for general assessment of lumbar spinal stenosis symptoms such as lower back and/or leg pain and discomfort. Score range from 0-10 (best-worst).[15,16]

Association between SSM pain / NRS and MRI parameters

For each patient there was one single value for each SSM pain and NRS, but MRI parameters were evaluated on five spinal levels (L1-L5). First, we searched for associations between MRI parameters in all five levels (full analysis). Second, we reduced each of the MRI parameters individually to the level with the most prominent value (restricted analysis).

Statistical analysis

We used descriptive statistics for the clinical findings, socio-demographic variables, and MRI parameters. For continuous variables, median and interquartile ranges were calculated; categorical variables were displayed as number and percentage of total. Graphical representations including scatter plots and Spearman correlation coefficients were used to search for an association between SSM pain / NRS and MRI measurements at baseline. Analyses were performed using the R statistical software for Windows.[17]

Results

Findings from the systematic review of the literature

Study characteristics

We identified two studies, including 138 patients, published 2011 and 2012 demonstrating an association between MRI parameters and pain. We identified two further studies, including 144 patients, published 2007 and 2013, which showed no association between MRI parameters and pain.

Findings

Table 1 summarizes the MRI and clinical parameters as well as the applied statistical method and the author's conclusion for both studies that found a relation. One study[18] used the degree (none, mild, moderate, severe) of stenosis (overall, central, lateral recess, foramen) as MRI parameter, the other study[7] the cross-sectional area (mm^2) of the dural sac. In both studies VAS was used to quantify pain. The statistical methods were different between both studies.

Table 2 summarizes the relevant information from the studies showing no association. One study[3] used the anteroposterior spinal canal diameter and the other study[6] a grading of canal stenosis (ratio: cerebrospinal fluid/rootlet, based on the method by Schizas[19]) as MRI parameters. The former assessed pain with VAS whereas the latter used the MPQ.

Association between SSM pain / NRS and most prominent MRI parameters in patients of the LSOS study

Patient characteristics

A total of 150 patients were included in this analysis (**Table 3**). Median patient age was 75 years (interquartile range (IQR): 67-80). Seventy-six patients were female (50.7%), and 99 (66%) suffered from symptoms more than twelve months. Of the study population 101 (67.3%) patients hold higher education degree (no university) and 17 (11.3%) hold a university degree. Median SSM pain was 4 (IQR: 3.3-4), and median NRS value was 7 (IQR: 5-8).

Results from lumbar spine MRIs

Descriptive statistics for radiologic parameters indicating lumbar spinal stenosis of the 150 patients are summarized in **Table 4**. To assess relationships between segment-wise MRI readouts and pain outcomes, we started with calculating Spearman correlation coefficients. In addition we produced scatterplots of these pairs. We only found very weak correlations between any MRI parameters and clinical outcomes. We restricted the analysis to the most prominent segment for the

five core[12] and three additional quantitative MRI parameters ("anteroposterior diameter of dural sac", "cross-sectional area of dural tube/sac", "depth of lateral recess (right/left)"). The Spearman correlation coefficients for the restricted analysis varied between -0.22 (compromise of the foraminal zone, left) and 0.1 (depth of lateral recess, right) for SSM pain. Similar values were found for the correlation with NRS: the Spearman correlations varied between -0.26 (foraminal nerve root impingement, left) and 0.24 (depth of lateral recess, right). The resulting scatterplots for the five core and three additional quantitive MRI parameters (resulting in 12 parameters when right/left was differentiated) read out by a senior radiologist (board certified, fellowship-trained, with 13 years in spinal imaging) versus SSM pain domain and NRS is shown in **Figures 2 and 3**.

Discussion

Main findings

The results of this paper are twofold. In the systematic review, including four papers about the associations between radiological findings in the MRI and pain, the authors of two articles reported no association and two of them did. Lavelle et al.[18] stated that the degree of stenosis, assessed by spine surgeons in the MRI, was associated with leg pain quantified by a Visual Analoge Scale (VAS). Sigmundsson et al.[7] reported a weak correlation between leg/back pain (VAS) and the size of the dural sac area. In the data of the LSOS study we could not identify a statistically relevant association between any of the multiple MRI parameters and buttock, leg and back pain, quantified by SSM pain. Even by restricting the analysis to the level of the lumbar spine with the most prominent radiological 'stenosis' no relevant association could be shown.

In contrast to our analysis the four studies[3,6,7,18] included in the systematic review assessed only up to three different MRI parameters with various clinical outcomes. The results of our study support the results of at least two of the earlier studies[3,6] whereas the other two studies found no strong associations.[7,18]

Implications for practice

In some patients the diagnosis of lumbar spinal stenosis is straightforward. At least in patients who complain about neurogenic claudication – pain in buttocks and/or legs provoked by walking or standing and relieved by sitting an bending forward – and a stenosis on only one spinal level verified by MRI. In such cases it seems reasonable to assume that the singular narrowing causes the symptoms and surgical decompression on the corresponding level will relieve symptoms of the patient with high probabilty. In many patients with neurgenic claudication the lumbar spine MRI shows not a singular stenosis, but rather stenoses on more than one level. In the SPORT's trial about 60% of included patients had moderate or severe stenoses on two or more levels of the lumbar spine.[20] In the LSOS cohort 43% had stenoses on more than one level. These multilocular stenoses in the MRI are a major challenge for the surgeons. So far MRI findings seem not to be very helpful to tell the surgeon which radiological findings are causal for the symptoms what makes it difficult to decide which stenoses the surgeon needs to decompress. The non-existent or weak association between radiological findings and symptoms might explain to some extent that more than one third of patients report no clinically relevant improvement after surgery.[20,21]

Implications for research

It is crucial to understand the causal associations between clinical symptoms and radiologic findings, in particular for spine surgeons in planning the kind of surgery. Multiple dependencies between the MRI parameters, measured at each of five spinal levels, require variable selection before model fitting. Due to the large number of potential multiple models, more sophisticated statistical methods like machine learning approaches or model averaging could be applied. Furthermore, other imaging procedures should be considered. The spinal canal is a dynamic structure and the diameters vary by changing posture and by bodily activities.[6] Consequently, a static image of the lumbar canal in the supine (position) may not represent the dimensions of the spinal canal during standing or walking. Another approach to get to know more about why these

patients suffer from intermittent episodes of pain could be the assessment of blood circulation in the spinal region or the functional assessment of the nerve roots and peripheral nerves. It is assumed and some evidence supports the thesis that obstruction of the blood circulation – arterial and/or venous – is causal for the intermittent character of the pain.[22] Nerve function might be assessed by new imaging modalities such as high resolution MR neurography or diffusion tensor imaging.[23,24] These latter approaches might raise the question wheter morphological-based MRI parameters represent valuable biomarkers at all.

Strengths and limitations

One limitation of this study is that different MRI scanners were in charge for the image acquisition of the multicenter LSOS study, which could have lead to to some bias as only standard sagittal T1 and T2 weighted as well as axial T2 weighted images were available for image analysis. Fat-suppressed fluid-sensitive MR images are considered standard of care for lumbar spine imaging but they have not been implemented in all participating study centers of the LSOS study and were thus not considered mandatory for this study population. However, with respect to the recent literature and to our own experience, we recommend the inclusion of fluid-sensitive MRI sequences (such as Short-Tau Inversion Recovery [STIR] sequences) in patients with known or suspected LSS to detect unexpected subtle fractures, tumor involvement or Modic 1 end-plate changes of the lumbar spine.[25-27] Furthermore, MRI scans were performed in supine position which is currently standard of care. In addition, we did not investigate into the inter-reader reliability of the MRI image analysis.

Our study has several strengths. The 23 MRI parameters which we used for the evaluation of our own data, were predefined in an international consensus meeting[12] and based on the best available evidence in the literature.[28-30] Compared to studies analysed in the systematic review, our approach included eight different MRI parameters. In addition to the frequently used NRS or VAS, respectively, our study was the only one that measured pain with the pain domain subscale of the

SSM as recommended by the North American Spine Society (NASS)[31] to be the "gold standard" to quantify complaints in patients with lumbar spinal stenosis. However, complaints of pain severity are extremely subjective and depend on the individual processing of nociceptive information.[32,33]

Conclusion

Despite a thorough analysis of the data we were not able to prove any correlation between radiological findings (MRI) and the severity of pain. There is a need for innovative 'methods/techniques' to learn more about the causal relationship between radiological findings and the patients' pain related complaints.

Acknowledgments

The authors thank the Baugarten Foundation, the Helmut Horten Foundation, the Pfizer-Foundation for geriatrics & research in geriatrics, the Symphasis Charitable Foundation, and the OPO Foundation for their support. Thanks are extended to Dr. Martina Gosteli, University of Zurich, for conducting the literature search.

Appendix 1: Search History for Embase May 2014

#	Query	Results
1	**'nuclear magnetic resonance imaging'**/exp	520’594
2	((**'magnetization transfer'** OR **'magnetisation transfer'** OR **'magnetic resonance'** OR **mr** OR **nmr** OR **'proton spin'** OR **'chemical shift'**) NEAR/3 (**imaging** OR **tomography**)):ab,ti	198’652
3	**#1** OR **#2**	543’591
4	**'hospital anxiety and depression score'**:ab,ti OR **'spinal stenosis measurement'**:ab,ti OR **'fear avoidance believes questionnaire'**:ab,ti OR **'hopkins scl-k-9'**:ab,ti OR **'hopkins symptom checklist short version-9'**:ab,ti OR **'euroquol'**:ab,ti OR **'roland and morris questionnaire'**:ab,ti OR **'core outcome measures index'**:ab,ti OR **'oswestry disability index'**:ab,ti OR **'short-form 36'**:ab,ti	10’011
5	**hads**:ab,ti OR **ssm**:ab,ti OR **fabq**:ab,ti OR **fess**:ab,ti OR **'eq 5d'**:ab,ti OR **rmq**:ab,ti OR **rdq**:ab,ti OR **comi**:ab,ti OR **omi**:ab,ti OR **'sf 36'**:ab,ti	29’906
6	**'short form 36'**/exp	11’736
7	**'questionnaire'**/exp	390’522
8	((**scoring** OR **rating** OR **measur*** OR **assess***) NEAR/3 (**scale** OR **system**)):ab,ti	118’978
9	((**scor*** OR **rating** OR **measur*** OR **assess***) NEAR/5 (**pain** OR **function** OR **satisfaction**)):ab,ti	199’068
10	**#4** OR **#5** OR **#6** OR **#7** OR **#8** OR **#9**	684’079
11	**#3** AND **#10**	16’036
12	**'backache'**/exp OR **'spine disease'**/exp	201’429
13	**'back pain'**:ab,ti OR **'back pains'**:ab,ti OR **'back ache'**:ab,ti OR **'back aches'**:ab,ti OR **backache***:ab,ti	41’123
14	((**lowback** OR **lumbal** OR **lumbar** OR **lumbosacral**) NEAR/3 (**pain*** OR **ache*** OR **syndrome**)):ab,ti	5’276
15	**lumbago**:ab,ti OR **lumbalgia**:ab,ti OR **lumbalgesia**:ab,ti OR (**lumbosacroiliac** NEAR/3 **strain**):ab,ti	1’779
16	(**'intervertebral disc'** NEAR/3 (**degeneration** OR **displacement**)):ab,ti	1’213
17	(**spinal** NEAR/3 (**curvatures** OR **stenosis** OR **osteochondrosis**)):ab,ti	5’075

18	**spondylitis**:ab,ti OR **spondylosis**:ab,ti	19’438
19	**#12** OR **#13** OR **#14** OR **#15** OR **#16** OR **#17** OR **#18**	210’920
20	**#11** AND **#19**	1’544
21	**'backache'**/exp/dm_ep	2’573
22	**'spine disease'**/exp/dm_ep	3’927
23	**#21** OR **#22**	6’295
24	**'epidemiology'**/de OR **'morbidity'**/de OR **'incidence'**/exp OR **'prevalence'**/exp	949’826
25	**associat***:ti OR **caus***:ti OR **epidemiol***:ti OR **correlat***:ti OR **relat***:ti	1’725’329
26	**#24** OR **#25**	2’534’701
27	**#23** AND **#26**	3’284
28	**#3** AND **#27**	243
29	**#20** OR **#28**	1’774
30	**#20** OR **#28** AND [animals]/lim	27
31	**#20** OR **#28** AND [animals]/lim AND [humans]/lim	15
32	**#30** NOT **#31**	12
33	**#29** NOT **#32**	1’762
34	**#29** NOT **#32** AND [1998-2014]/py	1’694
35	**#34** AND **'case report'**/de	74
36	**#34** NOT **#35**	1’620
37	**#36** AND **'conference abstract'**/it	387
38	**#36** NOT **#37**	1‘233

Appendix 2: MRI parameters per level (according to Andreisek et al.[12])

No	MRI Parameter	Classification / Parameter Description	Reference
1	Segment Fracture	Yes / No	
2	Discus grading (Pfirrmann classification)	Grade 1-5 according to structure, distinction of nucleus/anulus, signal intensity, and height of the disc	~~31~~34
3	Modic classification	Normal; Modic 1: bone marrow oedema; 2: bone marrow conversion into fatty marrow; 3: sclerosis	~~32~~35
4	Listhesis	Yes / No	~~33~~36
5	Osteoarthritis facet joint right	Yes / No	~~34,35~~37,38
6	Osteoarthritis facet joint left	Yes / No	~~34,35~~37,38
7	Flavum hypertrophy right	Yes / No	~~34~~37
8	Flavum thickness right	Measured in millimeters [mm]	~~41,43~~37,39
9	Flavum hypertrophy left	Yes / No	~~34~~37
10	Flavum thickness left	Measured in millimeters [mm]	~~41,43~~37,39
11	Lipomatosis grading (Borré classification)	Grade 0: normal amount of epidural fat; 1: mild, 2: moderate; 3: severe epidural fat overgrowth	~~36~~40
12	Compromise of central zone	No: no compromise; mild: compromise of ≤1/3; moderate: compromise of 1/3 – 2/3; severe: compromise of >2/3 of its normal size	~~37~~41
13	Relation between fluid and cauda equine	Grading based on the rootlet/cerebrospinal fluid ratio in axial MRI images. Grades A1-A4 and B show cerebrospinal fluid presence while grades C and D show none at all	19
14	Foraminal nerve root impingement right	Contact of disc material with nerve root; Grade 0: normal; 1: contact; 2: deviation; 3: compression	~~38~~42
15	Foraminal nerve root impingement left	see parameter No.14	~~38~~42
16	Nerve root compression in the lateral recess right	Grade 0: no narrowing; 1: narrowing, but no root compression; 2: significant narrowing with the nerve root flattened but with preservation of cerebrospinal fluid; 3: severe root compression	~~39~~43
17	Nerve root compression in the	see parameter No.16	~~39~~43

	lateral recess left		
18	Compromise of the foraminal zone right	No: no compromise; mild: compromise of ≤1/3; moderate: compromise of 1/3 – 2/3; severe: compromise of >2/3 of its normal size	~~37~~41
19	Compromise of the foraminal zone left	see parameter No. 18	~~37~~41
20	Anteroposterior diameter of dural sac	Measured in millimeters [mm]	~~44,45~~46,47
21	Cross-sectional area of dural tube/sac	Measured in square millimeters [mm^2]	~~46,47~~42,43
22	Depth of lateral recess right	Measured in millimeters [mm]	~~48,49~~42,43
23	Depth of lateral recess left	Measured in millimeters [mm]	~~48,49~~42,43

References

1. Deyo RA. Treatment of lumbar spinal stenosis: a balancing act. *The spine journal : official journal of the North American Spine Society* 2010;10:625-7.

2. Kreiner DS, Shaffer WO, Baisden JL, et al. An evidence-based clinical guideline for the diagnosis and treatment of degenerative lumbar spinal stenosis (update). *Spine Journal* 2013;13:734-43.

3. Geisser ME, Haig AJ, Tong HC, et al. Spinal canal size and clinical symptoms among persons diagnosed with lumbar spinal stenosis. *Clinical Journal of Pain* 2007;23:780-5.

4. Haig AJ, Tong HC, Yamakawa KS, et al. Spinal stenosis, back pain, or no symptoms at all? A masked study comparing radiologic and electrodiagnostic diagnoses to the clinical impression. *Archives of Physical Medicine & Rehabilitation* 2006;87:897-903.

5. Jensen MC, Brant-Zawadzki MN, Obuchowski N, et al. Magnetic resonance imaging of the lumbar spine in people without back pain. *N Engl J Med* 1994;331:69-73.

6. Kim HJ, Suh BG, Lee DB, et al. The influence of pain sensitivity on the symptom severity in patients with lumbar spinal stenosis. *Pain Physician* 2013;16:135-44.

7. Sigmundsson FG, Kang XP, Jonsson B, et al. Correlation between disability and MRI findings in lumbar spinal stenosis: a prospective study of 109 patients operated on by decompression. *Acta Orthopaedica* 2011;82:204-10.

8. Ishimoto Y, Yoshimura N, Muraki S, et al. Associations between radiographic lumbar spinal stenosis and clinical symptoms in the general population: the Wakayama Spine Study. *Osteoarthritis & Cartilage* 2013;21:783-8.

9. Boden SD, Davis D, Dina T, et al. Abnormal magnetic-resonance scans of the lumbar spine in asymptomatic subjects. A prospective investigation. *The Journal of Bone & Joint Surgery* 1990;72:403-8.

10. Steurer J, Nydegger A, Held U, et al. LumbSten: the lumbar spinal stenosis outcome study. *BMC musculoskeletal disorders* 2010;11:254.

11. Thomas Reuters (Scientific) LLC. EndNote [EndNote], 2015. Available at: http://www.endnote.com/, 2015.

12. Andreisek G, Deyo RA, Jarvik JG, et al. Consensus conference on core radiological parameters to describe lumbar stenosis - an initiative for structured reporting. *European radiology* 2014.

13. Stucki G, Daltroy L, Liang MH, et al. Measurement properties of a self-administered outcome measure in lumbar spinal stenosis. *Spine* 1996;21:796-803.

14. Wertli MM, Steurer J, Wildi LM, et al. Cross-cultural adaptation of the German version of the spinal stenosis measure. *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society* 2014;23:1309-19.

15. Downie WW, Leatham PA, Rhind VM, et al. Studies with pain rating scales. *Ann Rheum Dis* 1978;37:378-81.

16. Kremer E, Atkinson JH, Ignelzi RJ. Measurement of pain: patient preference does not confound pain measurement. *Pain* 1981;10:241-8.

17. R Development Core Team. R: A language and environment for statistical computing. [R: A language and environment for statistical computing], 2011. Available at: http://www.R-project.org/, 2013.

18. Lavelle WF, Tallarico R, Madom IA, et al. Comparison of surgeon assessed stenosis and validated patient functional outcome scores. *Spine Journal* 2012;12:117S-8S.

19. Schizas C, Theumann N, Burn A, et al. Qualitative grading of severity of lumbar spinal stenosis based on the morphology of the dural sac on magnetic resonance images. *Spine* 2010;35:1919-24.

20. Weinstein JN, Tosteson TD, Lurie JD, et al. Surgical versus nonoperative treatment for lumbar spinal stenosis four-year results of the Spine Patient Outcomes Research Trial. *Spine* 2010;35:1329-38.

21. Atlas SJ, Keller RB, Wu YA, et al. Long-term outcomes of surgical and nonsurgical management of lumbar spinal stenosis: 8 to 10 year results from the maine lumbar spine study. *Spine* 2005;30:936-43.

22. Kobayashi S, Suzuki Y, Meir A, et al. Circulatory dynamics of the cauda equina in lumbar canal stenosis using dynamic contrast-enhanced magnetic resonance imaging. *The spine journal : official journal of the North American Spine Society* 2015.

23. Eppenberger P, Andreisek G, Chhabra A. Magnetic resonance neurography: diffusion tensor imaging and future directions. *Neuroimaging Clin N Am* 2014;24:245-56.

24. Birnbaum J, Duncan T, Owoyemi K, et al. Use of a novel high-resolution magnetic resonance neurography protocol to detect abnormal dorsal root Ganglia in Sjogren patients with neuropathic pain: case series of 10 patients and review of the literature. *Medicine (Baltimore)* 2014;93:121-34.

25. Lalkadamyali H, Tarhan NC, Ergun T, et al. STIR Sequence for Depiction of Degenerative Changes in Posterior Stabilizing Elements in Patients with Lower Back Pain. *Am J Roentgenol* 2008;191:973-9.

26. Del Grande F, Santini F, Herzka DA, et al. Fat-suppression techniques for 3-T MR imaging of the musculoskeletal system. *Radiographics* 2014;34:217-33.

27. Gellhorn AC, Katz JN, Suri P. Osteoarthritis of the spine: the facet joints. *Nat Rev Rheumatol* 2013;9:216-24.

28. Andreisek G, Imhof M, Wertli M, et al. A systematic review of semiquantitative and qualitative radiologic criteria for the diagnosis of lumbar spinal stenosis. *AJR. American journal of roentgenology* 2013;201:W735-46.

29. Mamisch N, Brumann M, Hodler J, et al. Radiologic criteria for the diagnosis of spinal stenosis: results of a Delphi survey. *Radiology* 2012;264:174-9.

30. Steurer J, Roner S, Gnannt R, et al. Quantitative radiologic criteria for the diagnosis of lumbar spinal stenosis: a systematic literature review. *BMC musculoskeletal disorders* 2011;12:175.

31. Watters WC, Baisden J, Gilbert TJ, et al. Degenerative lumbar spinal stenosis: an evidence-based clinical guideline for the diagnosis and treatment of degenerative lumbar spinal stenosis. *The spine journal* 2008;8:305-10.

32. Edwards RR, Sarlani E, Wesselmann U, et al. Quantitative assessment of experimental pain perception: multiple domains of clinical relevance. *Pain* 2005;114:315-9.

33. Ruscheweyh R, Verneuer B, Dany K, et al. Validation of the pain sensitivity questionnaire in chronic pain patients. *Pain* 2012;153:1210-8.

34. Pfirrmann CWA, Metzdorf A, Zanetti M, et al. Magnetic resonance classification of lumbar intervertebral disc degeneration. *Spine* 2001;26:1873-8.

35. Modic MT, Steinberg PM, Ross JS, et al. Degenerative disk disease: assessment of changes in vertebral body marrow with MR imaging. *Radiology* 1988;166:193-9.

36. Kauppila LI, Eustace S, Kiel DP, et al. Degenerative displacement of lumbar vertebrae. A 25-year follow-up study in Framingham. *Spine* 1998;23:1868-73; discussion 73-4.

37. Grenier N, Kressel HY, Schiebler ML, et al. Normal and degenerative posterior spinal structures: MR imaging. *Radiology* 1987;165:517-25.

38. Kalichman L, Hunter DJ. Lumbar facet joint osteoarthritis: a review. *Seminars in arthritis and rheumatism* 2007;37:69-80.

39. Park JB, Chang H, Lee JK. Quantitative analysis of transforming growth factor-beta 1 in ligamentum flavum of lumbar spinal stenosis and disc herniation. *Spine* 2001;26:E492-5.

40. Borre DG, Borre GE, Aude F, et al. Lumbosacral epidural lipomatosis: MRI grading. *European radiology* 2003;13:1709-21.

41. Lurie JD, Tosteson AN, Tosteson TD, et al. Reliability of readings of magnetic resonance imaging features of lumbar spinal stenosis. *Spine* 2008;33:1605-10.

42. Pfirrmann CWA, Dora C, Schmid MR, et al. MR image-based grading of lumbar nerve root compromise due to disk herniation: Reliability study with surgical correlation. *Radiology* 2004;230:583-8.

43. Bartynski WS, Lin L. Lumbar root compression in the lateral recess: MR imaging, conventional myelography, and CT myelography comparison with surgical confirmation. *Am J Neuroradiol* 2003;24:348-60.

44. Jonsson B, Annertz M, Sjoberg C, et al. A prospective and consecutive study of surgically treated lumbar spinal stenosis. Part I: Clinical features related to radiographic findings. *Spine* 1997;22:2932-7.

45. Kalichman L, Cole R, Kim DH, et al. Spinal stenosis prevalence and association with symptoms: the Framingham Study. *The spine journal : official journal of the North American Spine Society* 2009;9:545-50.

46. Hamanishi C, Matukura N, Fujita M, et al. Cross-sectional area of the stenotic lumbar dural tube measured from the transverse views of magnetic resonance imaging. *J Spinal Disord* 1994;7:388-93.

47. Laurencin CT, Lipson SJ, Senatus P, et al. The stenosis ratio: a new tool for the diagnosis of degenerative spinal stenosis. *International journal of surgical investigation* 1999;1:127-31.

Figure 1. Study flow

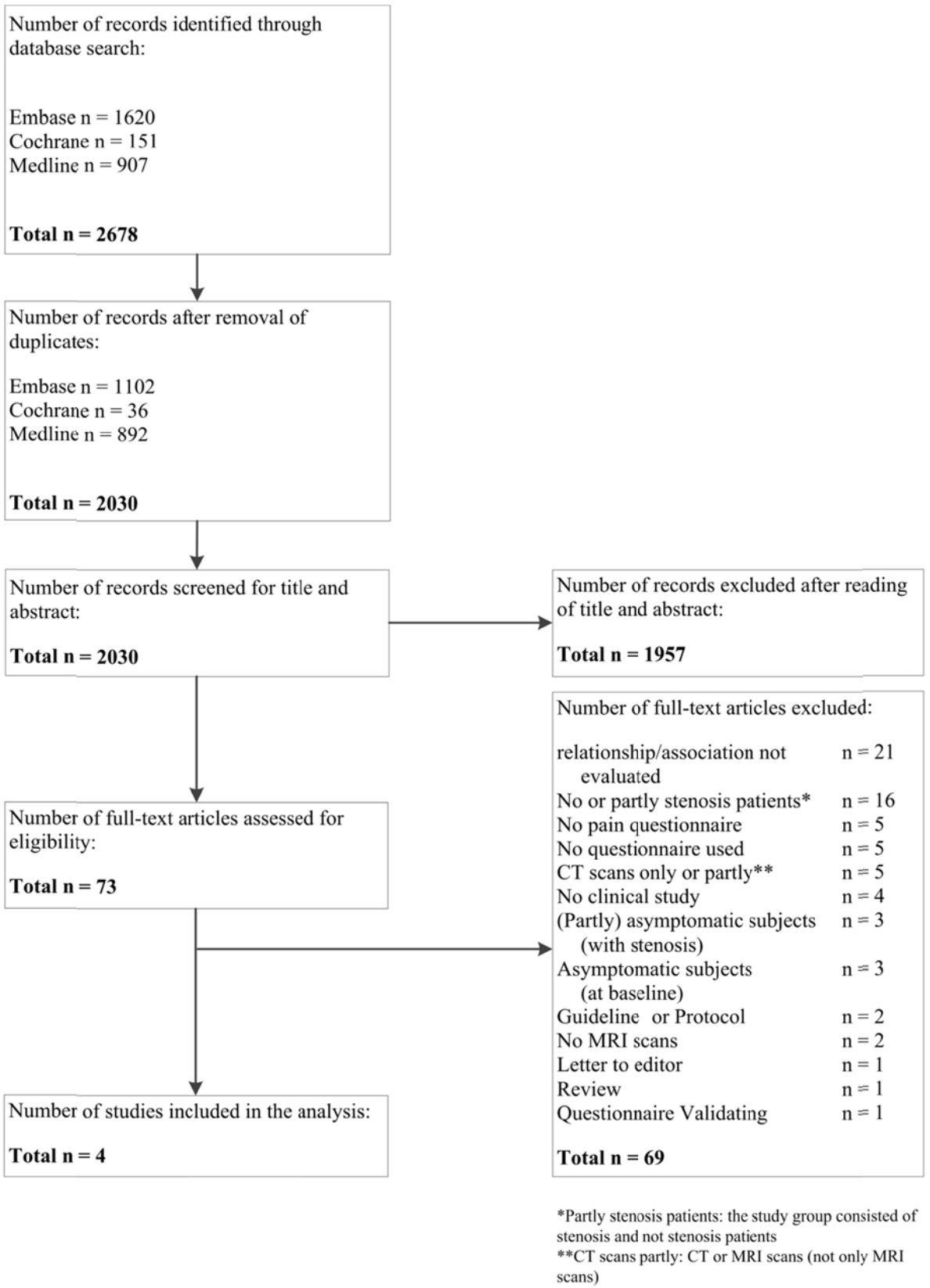

Figure 2. Scatter plots of Spinal Stenosis Measure (SSM) Pain Domain against each of the five core and three additional quantitive MRI parameters. Most extreme value (maximum or minimum) over the five spinal levels is plotted for each MRI variable. Spearman correlation coefficient = r.

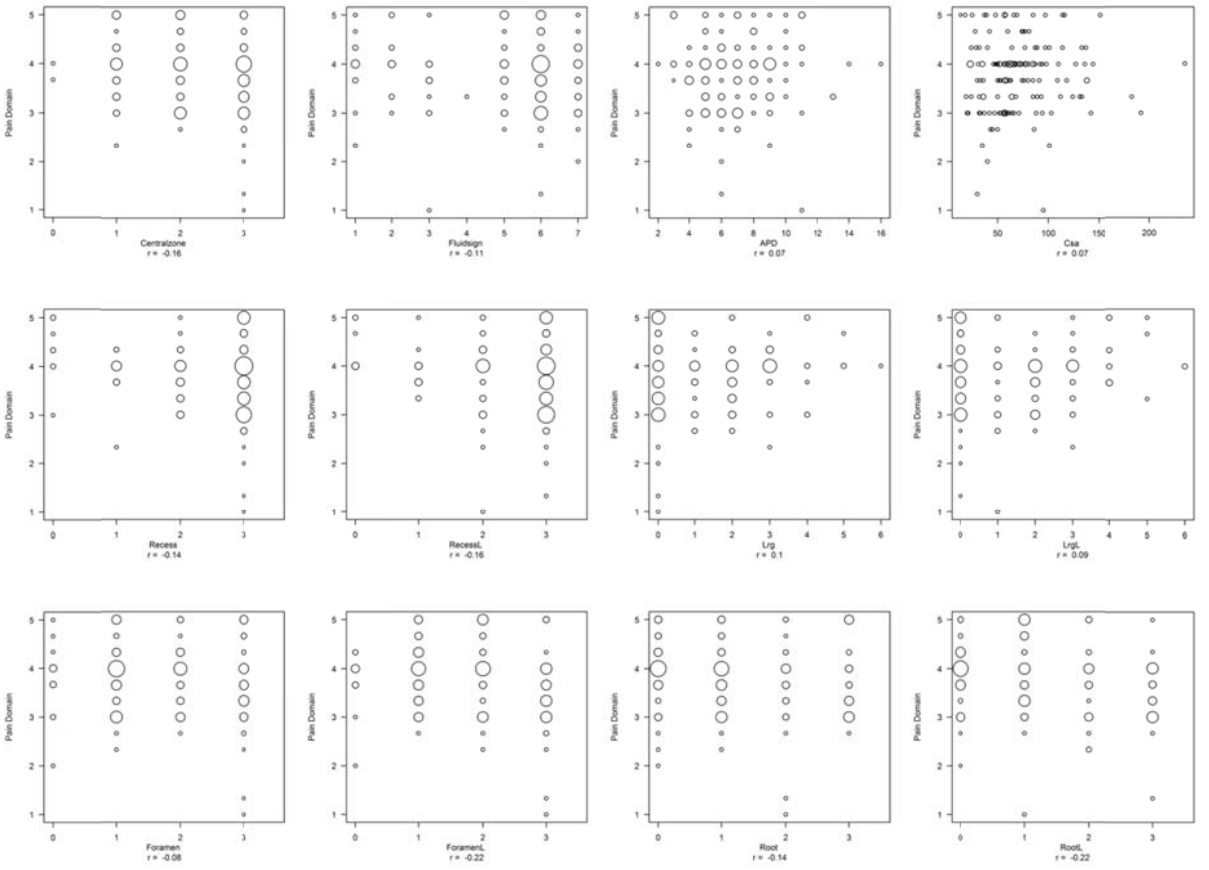

Figure 3. Scatter plot of Numeric Rating Scale (NRS) against each of the five core and three additional quantitive MRI parameters. Most extreme value (maximum or minimum) over the five spinal levels is plotted for each MRI variable. Spearman correlation coefficient = r.

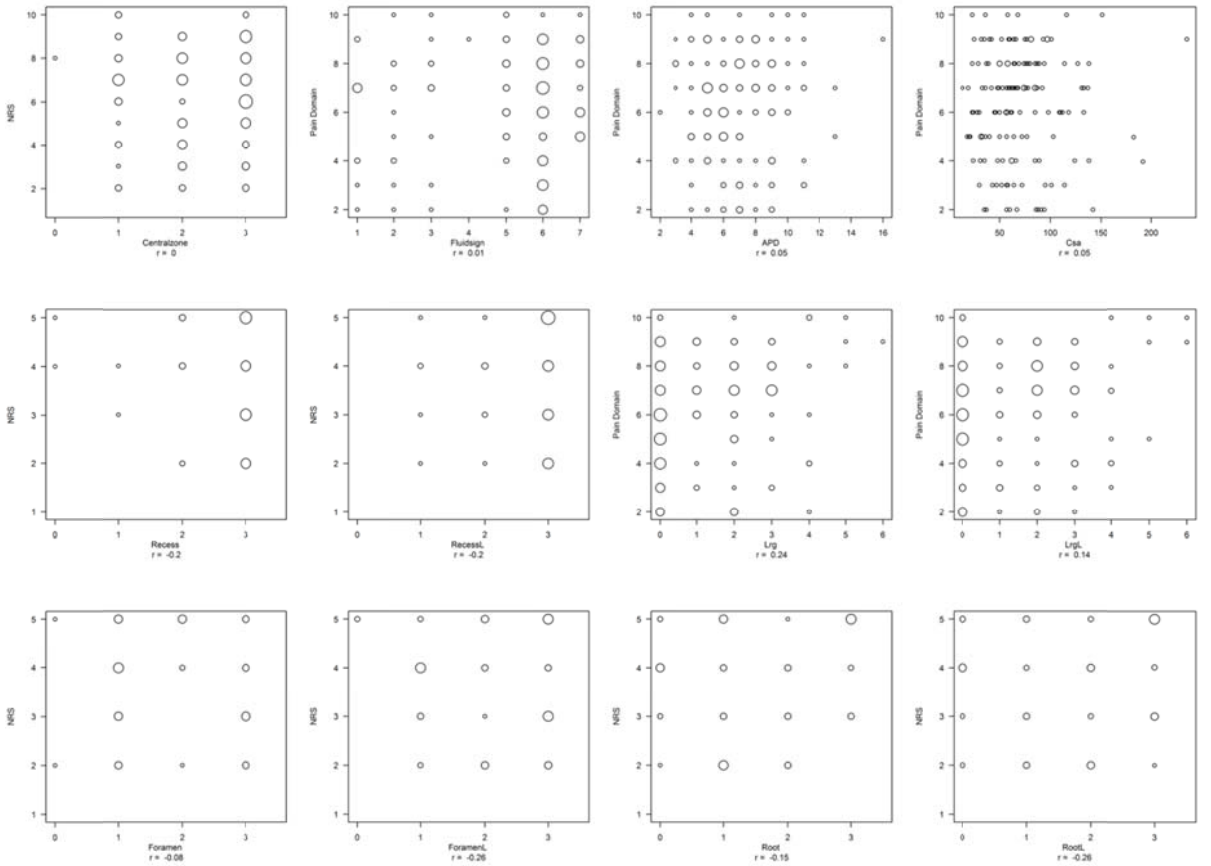

Table 1: Summary of studies that found a specific relation between MRI parameters and clinical parameters

Study, year	MRI parameter	Clinical parameter	Statistical method	Result/conclusion
Lavelle, 2012[18]	Degree of stenosis (none, mild, moderate, severe)	VAS leg pain	Linear regression	VAS leg pain was found to correlate well with surgeon assessed MRI imaging findings (overall stenosis p=0.012, central p =0.05, lateral recess p=0.023, foramen p=0.074).
Sigmundsson, 2011[7]	Cross-sectional area of the dural sac (mm^2)	VAS (100 mm) low back / leg pain	Pearson's correlation	Patients with multilevel stenosis had better general health (p = 0.04) and less leg and back pain despite having smaller dural sac area than patients with single-level stenosis. There was a poor correlation between walking distance, ODI, the SF-36, EQ-5D, and leg and back pain levels on the one hand and dural sac area on the other.

MRI: magnetic resonance imaging; ODI: Oswestry Disability Index; VAS: Visual Analog Scale

Table 2: Summary of studies that found no specific relation between MRI parameters and clinical parameters

Study, year	MRI parameter	Clinical parameter	Statistical method	Result/conclusion
Geisser, 2007[3]	Osseous anteroposterior spinal canal diameter	MPQ	Pearson's correlation	Anteroposterior spinal canal diameter is not predictive of clinical symptoms associated with lumbar spinal stenosis. (Anterior-posterior spinal canal diameter was not significantly associated with any of the clinical symptom measures examined.)
Kim, 2013[6]	Grading of canal stenosis (ratio: cerebrospinal fluid / rootlet, based on the method by Schizas[19])	VAS (100 mm) back / leg pain	Analysis of variance	There was no significant association between the grade of canal stenosis and VAS for back pain/leg pain and ODI.

MPQ: McGill Pain Questionnaire; ODI: Oswestry Disability Index; VAS: Visual Analog Scale

Table 3: Baseline characteristics of the 150 patients of the LSOS study

Characteristics (n = 150)	
Age, median (IQR) (years)	75 (67-80)
Gender, n (%)	
Female	76 (50.7)
Male	74 (49.3)
Height, median (IQR) (cm)	168 (160−174.8)
Weight, median (IQR) (kg)	78 (67.3−89.3)
BMI, median (IQR) (kg/m^2)	26.7 (24−30.5)
Educational level, n (%)	
Compulsory education	31 (20.7)
High school	101 (67.3)
College, university	17 (11.3)
Not specified	1 (0.7)
Duration of symptoms, n (%)	
<3 months	11 (7.3)
3-6 months	16 (10.7)
6-12 months	18 (12)
>12 months	99 (66)
Not specified	6 (4)
CIRS total score, median (IQR)	10 (6.5−12.5)
SSM, median (IQR)	
SSM Pain domain	4 (3.3−4)
NRS	7 (5−8)

BMI: Body Mass Index; CIRS: Cumulative Illness Rating Scale; IQR: interquartile range;

NRS: Numeric Rating Scale; SSM: Spinal Stenosis Measure

Table 4: Baseline MRI parameters of the 150 patients of the LSOS study measured at each of five segments (read out by senior radiologist)

MRI parameter	**n segments analyzed**	
Axial images not available, n segments (%)		89 (11.9)
Segment fracture, n segments (%)	750	20 (2.7)
Discus grading (Pfirrman classification), n segments (%)	747	
Grade 1		12 (1.6)
Grade 2		96 (12.9)
Grade 3		202 (27)
Grade 4		303 (40.6)
Grade 5		134 (17.9)
Modic classification, n segments (%)	750	
Normal		448 (59.7)
1		33 (4.4)
2		258 (34.4)
3		11 (1.5)
Listhesis, n segments (%)	750	115 (15.3)
Osteoarthritis facet joint *right*, n segments (%)	654	502 (76.8)
Osteoarthritis facet joint *left*, n segments (%)	655	503 (76.8)
Flavum hypertrophy *right*, n segments (%)	656	353 (53.8)
Flavum thickness *right*, median (IQR) (mm)	654	5 (4-6)
Flavum hypertrophy *left*, n segments (%)	656	360 (54.9)
Flavum thickness *left*, median (IQR) (mm)	655	5 (4-6)
Lipomatosis grade (Borré classification), n segments (%)	662	
Grade 0		593 (89.6)
Grade 1		62 (9.4)
Grade 2		6 (0.9)
Grade 3		1 (0.2)
Compromise of central zone, n segments (%)	659	
no		129 (19.6)
mild		314 (47.6)
moderate		119 (18.1)
severe		97 (14.7)
Relation from fluid to cauda equina, n segments (%)	659	
Grade A1		291 (44.2)

Grade A2		95 (14.4)
Grade A3		74 (11.2)
Grade A4		14 (2.1)
Grade B		61 (9.3)
Grade C		97 (14.7)
Grade D		27 (4.1)
Nerve root compression in the lateral recess *right*, n segments (%)	659	
Grade 0		225 (34.1)
Grade 1		193 (29.3)
Grade 2		97 (14.7)
Grade 3		144 (21.9)
Nerve root compression in the lateral recess *left*, n segments (%)	659	
Grade 0		216 (32.8)
Grade 1		196 (29.7)
Grade 2		98 (14.9)
Grade 3		149 (22.6)
Foraminal nerve root impingement *right*, n segments (%)	750	
Grade 0		558 (74.4)
Grade 1		113 (15.1)
Grade 2		39 (5.2)
Grade 3		40 (5.3)
Foraminal nerve root impingement *left*, n segments (%)	750	
Grade 0		575 (76.7)
Grade 1		108 (14.4)
Grade 2		32 (4.3)
Grade 3		35 (4.7)
Compromise of the foraminal zone *right*, n segments (%)	750	
no		333 (44.4)
mild		245 (32.7)
moderate		99 (13.2)
severe		73 (9.7)
Compromise of the foraminal zone *left*, n segments (%)	749	
no		320 (42.7)
mild		259 (34.6)
moderate		108 (14.4)
severe		62 (8.3)
Anteroposterior diameter of dural sac, median (IQR) (mm)	659	10 (8-12)

Cross-sectional area of dural tube/sac, median (IQR) (mm^2)	659	120 (80-168)
Depth of lateral recess *right*, median (IQR) (mm)	659	4 (2-5)
Depth of lateral recess *left*, median (IQR) (mm)	659	3 (2-5)

IQR: interquartile range